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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,374	01/29/2004	Avi Ashkenazi	39780-1216 RICID1	4761

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/767,374	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *14 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *52,54,55 and 57-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52, 54-55, 57-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 3/14/06, is acknowledged.

2. Claims 52, 54-55 and 57-59 are pending and under examination in the instant application.

3. The following new ground of rejection is necessitated by the amendment submitted 3/14/06.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 52 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "exhibits anti-inflammatory properties" claimed in claim 52, lines 8-9 represents a departure from the specification and the claims as originally filed.

Applicant's amendment filed 3/14/06 points to the specification at page 42, lines 17-20 for support for the newly added limitation "exhibits anti-inflammatory properties" as claimed in claim 52. However, the specification does not provide a clear support for such limitation. It is noted that the specification on page 42, lines 17-20 discloses that the polypeptide of the present invention may be used to treat various inflammatory diseases and conditions, such as T cell mediated disease, including those characterized by infiltration of leucocytes cells into tissue, stimulation of T-cell proliferation, inhibition of T-cell proliferation, increased or decreased vascular permeability or the inhibition thereof. While this assertion is too nebulous, page 42, lines 21-23, specifically discloses that the proinflammatory nature of the compounds (e.g., PRO362) of the invention is indicated in the in vitro assays below. Also example 6 of the specification, table 3 discloses that claimed SEQ ID NO: 2 scored as positive for proinflammatory activity. Therefore, the PRO362 exhibits proinflammatory properties rather than anti-inflammtory properties. The instant claims now recite a limitation which was not clearly disclosed in the specification and recited in the claims as originally filed.

6. In view of the amendment filed on 3/14/06, only the following rejections are remained.

7. 35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

8. Claims 52, 54-55 and 57-59 stand rejected to under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the same reasons set forth in the previous Office Action mailed 9/14/05.

Applicant's arguments, filed 3/14/06, have been fully considered, but have not been found convincing.

Applicant refers to Dr. Menno van Lookeren declaration under 37 C.F.R. 1.132 which shows that treatment with the murine PRO362-Fc fusion protein: (1) resulted in significant reduction in joint swelling (Figure 1, Exhibit D), (2) inhibited joint inflammation (Fig 2, Exhibit E), (3) preserved cortical bone volume in the treated mice (figure 3, exhibit F), (4) did not alter the number nor the morphology of tissue resident macrophages (Figure 4, Exhibit G), (5) did not affect serum anti-collagen antibody titers (Figure 5, Exhibit H) and decreased the number of circulating inflammatory macrophages (Figure 6, Exhibit I).

However, such utility is not asserted in the specification as originally filed. The specification asserts that the proinflammatory nature of the compounds (e.g., PRO362) of the invention is indicated in the *in vitro* assays below (see page 42, lines 21-23). Further, the specification asserts that the invention relates to a method of treating an inflammatory disease, by administration of an effective therapeutic amount of a PRO362 *antagonist* to a patient in a patient in need thereof for the treatment of rheumatoid arthritis and other inflammatory disease (see page 4, lines 19-22). Also, the specification on page 55, Example 6 asserts that the polypeptides of the invention are proinflammatory (i.e., to induce inflammatory cell infiltrate) in that they stimulate inflammatory cell infiltrated (i.e., neutrophilic, eosinophilic, monocytic or lymphocytic) into guinea pig skin. Table 3 on page 55 asserts that DNA45416 protein of claimed SEQ ID NO: 2 scored positive for proinflammatory activity. However, the declaration states that the claimed polypeptide of SEQ ID NO: 2 has anti-inflammatory activities. Thus, Dr. van Lookeren's declaration is contradictory and provides mutually exclusive function regarding the asserted activity of the claimed PRO362 polypeptide of SEQ ID NO: 2 (i.e., anti-inflammatory vs. proinflammatory properties).

Applicant's attention is directed to *In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) quoting the Board of Patent Appeals,

> "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use of the compound, adducing evidence intended to sow that a particular specific use would have been obvious to men skilled in the particular art to which this use relates."

See also Brenner V. Manson, 148 U.S.P.Q. 689 (1966), where the court held that: a patent is not a hunting license.... [i]t is not a reward for the search, but compensation for its successful conclusion.

9. Claims 52, 54-55 and 57-59 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Further, besides an isolated polypeptide comprising SEQ ID NO: 2 encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209620, and the polypeptide consisting of the amino acid sequence from amino acid position 1 to amino acid position X of SEQ ID NO: 2, wherein X is any amino acid from position 271 to position 280, the specification fails to provide any guidance as to how to make any isolated polypeptide "having at least 95% amino acid sequence identity" to the amino acid sequence of the polypeptide of SEQ ID NO: 2 in claim 52(a), the amino acid sequence from amino acid position 1 to amino acid position X of SEQ ID NO: 2, wherein X is any amino acid from position 271 to position 280 in claim 52(b) or the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209620 in claim 52(c); where said polypeptide molecule exhibits anti-inflammatory properties in claim 52. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 9/14/05.

Applicant's arguments, filed 3/14/06, have been fully considered, but have not been found convincing.

Applicant submits that claimed invention complies with the utility requirement, one skilled in the art would know how to use the claimed invention so that it would operate as intended without undue experimentation.

However, Examiner's position is the same as set forth above under 35 U.S.C. § 101.

Applicant submits that the specification provides methods for making polypeptide variants were well known in the art at the time the present invention was made. Further, such methods are specifically described, for example at page 20, lines 9-38 of the specification. Applicant concludes that at the time the present invention was made, one of ordinary skill would clearly have known how to make PRO362 variants, based on general knowledge in the art and the teaching of the specification, without undue experimentation. Applicant submits that positions for mutations without compromising biological activity could also have been identified, taking into account the structural information provided in the specification, e.g., in Example2, and further in view of the homology of the extracellular domain of PRO362 to that of JAM1 and the

A33 antigen. Similarly to JAM family members, PRO362 is a type I transmembrane molecule and a member of the IG superfamily. Applicant submits that the presence of motifs would have been readily recognized by those of ordinary skill in the art at the time the present invention was made. Applicant submits that sequences conserved between human and mouse PRO362 provide assistance in identifying sequences important for preserving biological activity. Applicant asserts that the one of ordinary skill in the art would also have known how to test such variants to determine whether they exhibit anti-inflammatory activity.

However, the claims as written encompass a broad genus of variants with a large number of possibilities with regard to the length of the amino acid sequence. Further, the specification does not appear to have provided sufficient guidance as to which variant of SEQ ID NO: 2 would share the biologically active variant of SEQ ID NO:2. Neither does Applicant appears to have provided any working examples of any variant. Thus it would require undue experimentation of the skilled artisan to determine which variants of SEQ ID NO:2 would have the biologically active variants of the full length molecule. It is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence and the functional properties of the different parts of the protein. Furthermore, in order to satisfy the U.S.C 112, first paragraph, the specification has to teach how to make and/or use the invention, not how to search for the invention. Until the time when such variants are identified, then one skill in the art can make them.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The

fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 24, 2006

Maher Haddad

Maher Haddad, Ph.D.
Patent Examiner